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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,642	12/08/2003	Laurent Mene-Saffrane	A36097-PCT-USA-A	5374

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EXAMINER	
IBRAHIM, MEDINA AHMED	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 05/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/731,642	MENE-SAFFRANE ET AL.	
	Examiner	Art Unit	
	Medina A. Ibrahim	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05/19/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 10/26/04

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5)☐ Notice of Informal Patent Application (PTO-152)

6)☐ Other: _____.

S.O.O.

DETAILED ACTION

Claims 1-21 are pending and are examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims1-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of transforming a plant with an expression vector comprising an isolated nucleic acid encoding SEQ ID NO: 1, for resistance against at least phytophthora parasitica nicotiana (Ppn), a transformed plant/cell comprising and an expression vector comprising said nucleic acid encoding SEQ ID NO: 1, does not reasonably provide enablement for any method for reducing sensitivity to a pathogen or a herbivore comprising overexpressing any lipoxygenase gene including 9-lipoxygenase from Solanacea or nucleic acids encoding a lipoxygenase having at least 80% or 90% sequence identity to SEQ ID NO: 1, expression cassette and plant/cell comprising said lipoxygenase gene or nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a method for reducing sensitivity to a pathogen or a herbivore comprising overexpressing any lipoxygenase gene including 9-lipoxygenase from Solanacea, or nucleic acids encoding a lipoxygenase that is at least

80% or 90% homologous to SEQ ID NO: 1 and having lipoxygenase activity, an expression cassette, a vector and transformed plant/cell comprising said lipoxygenase gene or nucleic acids operably linked to 35 CaMV.

Applicant teaches transformation of tobacco plants with an expression vector comprising CaMV promoter operably linked to a nucleotide sequence encoding SEQ ID NO: 1 (Example 5). The nucleotide sequence encoding SEQ ID NO: 1 is a known elicitor induced tobacco lipoxygenase. Applicant also teaches analysis of LOX transcript accumulation in the T1 transgenic tobacco plants as compared to control plants by Northern blotting (Example 7). Applicant further teaches measurement of LOX activity in transgenic and wild-type plants by using TLC and Spectrophotometer methods (Examples 10-11). Applicant also teaches stem inoculation of transgenic and wild-type tobacco plants with phytophthora parasitica nicotiana (Ppn); observation and quantification of symptoms, 6 or 11 days after inoculation (Examples 12-13); measurement of LOX1 transcript accumulation and LOX specific activity in the stems of T1 transgenic plants (Example 14); analysis of interaction between phytophthora parasitica nicotiana (Ppn) and T1 transgenic tobacco plants having constitutive LOX activity after stem and root inoculation (Examples 15-16). Results have indicated transgenic plants with much higher percentage of survival of as compared to the wild-type plants inoculated with same virulent race (Table 1).

Applicant, however, has not provided guidance for non-transformation methods of overexpressing a lipoxygenase gene in a plant. Applicant does not teach other than transforming a plant with a specific lipoxygenase gene. No guidance has been provided

for lipoxygenase genes other than the nucleotide sequences encoding SEQ ID NO: 1 having the ability to reduce plant sensitivity to exemplified or non-exemplified pathogens or herbivores. On page 13 of the specification (paragraph 0037), Applicant states that any lipoxygenase having the ability to reduce plant sensitivity to diseases when overexpressed in a plant can be used. However, Applicant has not taught how to identify lipoxygenase genes having such functional activity.

Kuhu et al (FEBS (1999), vol. 449, pp. 7-11) discuss about the diversity of the lipoxygenase family and the limited information available about their biological function. E. Blee (Prog. Lipid Res.(1998), Vol. 37 (1), pp. 33-72, Applicant's IDS) addresses plant lipoxygenase and their functional relevance. Blee specifically states "(I)nspite of considerable effort in the elucidation of the structure and the mechanism of plant lipoxygenases, their physiological functions are still a matter of debate (page 37, part 5). Blee continues" (C)early, the biochemical characterization of the different LOX isoforms and the identification of their distinct products are needed to identify the exact roles of these enzymes in the role phytooxylipin biosynthesis" (paragraph bridging pages 62 and 63). Also, Kolomiets et al (Plant Physiol. (2000), vol. 124, pp. 1121-1130, Applicant's IDS) state that identification of specific plant LOX genes involved in pathogen resistance is difficult because multiple LOX isozymes are involved in pathogen induced defense responses (see page 1122, column 1, 1st full paragraph). Therefore, it is clear that further research considered undue is required before one skilled will be able to use lipoxygenase encoding genes as broadly recited in the claims to reduce plant sensitivity to diseases in a transgenic plant.

On page 7 of the specification, Applicant reports possible phytotoxic property of lipoxygenases when overexpressed in plants. Deng et al (Planta (1992) 187:203-2089, Applicant's IDS) cited in Applicant's specification teaches that overexpression of lipoxygenase gene in a transgenic tobacco didn't result in the expected phenotype in the plant.

Furthermore, the working example disclosed in the specification is limited to the use of a nucleotide sequence encoding SEQ ID NO: 1, which is known in the prior art as an elicitor inducible lipoxygenase. Therefore, the ability of said nucleotide sequence to reduce plant sensitivity to Phytophthora parasitica (Ppn) cannot be extrapolated to other pathogens and herbivores, or to other lipoxygenase genes including those encoding polypeptides that are 80% or 90% homologous to SEQ ID NO: 1, absent further guidance. Applicant has not provided guidance for how and where to modify the nucleotide sequence encoding SEQ ID NO: 1 so that lipoxygenases that are 80% and 90% homologous as recited in the claims can be produced. Applicant has not disclosed a transgenic plant other than those overexpressing SEQ ID NO: 1. See *In re Fischer, 166 USPQ 19 24 (CCPA 1970)* where the court determined that the scope of the claims must bear a reasonable correlation with the scope of the enablement.

See also *Genentech Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997): The CAFC stated, "(P)atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable....While every aspect of generic claim certainly need not have been carried out by an inventor, or exemplified in the specification,

reasonable detail must be provided in order to enable members of the public to understand and carry out the invention....[w]hen there is no disclosure of any specific starting material or conditions under which a process can be carried out, undue experimentation is required..... It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement". Id. In this case, as in *Genentech*, the specification does not provide the "reasonable detail .....to enable members of the public to understand and carry out the invention" as broadly claimed.

Therefore, given the breadth of the claims, the nature of the invention, the state of the art, the unpredictability inherent regarding overexpression of lipoxygenase in a transgenic plant; the limited guidance and working examples as discussed supra, the claimed invention is not enabled throughout the broad scope. See In re Wands 858 F.2d 731, 8USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Claims 1-6, 8-13 and 15-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a method for reducing sensitivity to a pathogen or a herbivore comprising overexpressing any lipoxygenase gene including 9-lipoxygenase from Solanacea, or nucleic acids encoding a lipoxygenase that is at least

80% or 90% homologous to SEQ ID NO: 1 and having lipoxygenase activity, an expression cassette, a vector and transformed plant/cell comprising said lipoxygenase gene or nucleic acids operably linked to 35 CaMV. In contrast, Applicant describes transformation of plants with a nucleotide sequence encoding SEQ ID NO: 1, an expression cassette, a vector comprising said nucleotide sequence liked to CaMV promoter for overexpression, and plant/plant cell transformed with comprising said vector.

Applicant has not described a representative number of lipoxygenase capable of reducing plant sensitivity to pathogen and herbivores required for the claimed method and transformed plants/plant cells. In *Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), the court stated:

> An adequate written description of a DNA "requires a precise definition, such as by structure, formula, chemical name, or physical properties", not a mere wish or plan for obtaining the claimed chemical invention... Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it; what is required is a description of the DNA itself (43 USPQ2d at 1404).

The court held that held that human insulin-encoding cDNA is not described by prophetic example, which sets forth only a general method for obtaining the human cDNA:

> The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity...Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes...does not necessarily describe the DNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA....Accordingly, the specification does not provide a written description of human cDNA (43 USPQ2d at 1405).

The description of a single species of rat cDNA was held insufficient to describe the broad genera of vertebrate or mammalian insulin:

"In claims to genetic material...a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It doesn't define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function...does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is (43 USPQ2d at 1406).

The court continued:

"Thus...a cDNA is not defined by the mere name 'cDNA', even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA...A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus". (43 USPQ2d at 1406). See also where the court teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from the organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

The *University of Rochester v. G.D. Searle* & Co., Inc.(, U.S. District Court, Western District of New York, Decision and Order No. 00-CV-6161L,) decided 05 March 2003, at page 8, bottom paragraph, that method claims are properly subjected to a written description requirement if the starting material which requires that method is itself inadequately described. The court specifically stated, "(T)he claimed method depends upon finding a compound that selectively inhibits PGHS-2 activity. Without such a compound, it is impossible to practice the claimed method of treatment. It means little to "invent" a method if one does not have possession of a substance that is essential to practicing that method. Without that substance, the claimed invention is

more theoretical than real;..... and there is no meaningful possession of the method."

Applicant has not described structural elements common to all lipoxygenase genes capable of reducing plant sensitivity to pathogens and herbivores, and a literature review does not indicate that such structural elements or lipoxygenase are well known in the art. Consequently, the claimed methods that uses said lipoxygenase, vectors, expression vectors and transformed plants/cells comprising said genes are not adequately described.

Therefore, the claimed invention does not meet the current written description requirements. See, also, the Written description Examination Guidelines published in Federal Registry/Vol. 66, No.4/Friday, January 5, 2001/Notices).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 8-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Keller (US 5, 844, 121).

The claims are broadly drawn to a method for reducing sensitivity to a pathogen comprising overexpressing any lipoxygenase gene including plant 9-lipoxygenase in an expression cassette or a vector comprising said lipoxygenase operably linked to CaMV promoter for overexpression.

Keller teaches a method for producing transgenic plants having resistance to

fungal mycotoxin by transforming said plant with a vector comprising a gene encoding soybean 9-lipoxygenase under the control of the constitutive promoter CaMV promoter (column 3, last 2 full paragraphs; column 5, lines 26-36; and claims 1-9). Given the strong promoter, CaMV promoter used by Keller, overexpression of the lipoxygenase in the transgenic plant would be an inherent property.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over each of Keller (US 5, 844, 121) and Handa et al (WO 97/13851, Applicant's IDS) in

view of Veronesei et al (Plant Physiol (1996) 112:997-1004, Applicant's IDS).

The claims are broadly drawn to a method for reducing sensitivity to a pathogen or a herbivore comprising overexpressing any lipoxygenase gene including 9-lipoxygenase from Solanacea, or nucleic acids encoding a lipoxygenase that is at least 80% or 90% homologous to SEQ ID NO: 1 and having lipoxygenase activity, an expression cassette, a vector and transformed plant/cell comprising said lipoxygenase gene or nucleic acids operably linked to 35 CaMV.

Each of Keller and Handa teach transformation of plants with a lipoxygenase gene for a desired agronomic trait.

Keller teaches transformation of plants with a lipoxygenase gene for fungal resistance as discussed above.

Handa et al teach transformation of plants with a nucleotide sequence encoding tomato lipoxygenase for improved fruit quality, a plant expression vector/cassette comprising said nucleotide sequence operably linked to CaMV promoter (pages 10-11 and 17-20). Handa also teaches transformed plant and plant cells expressing said lipoxygenase (pages 21-22 and claims on page 24-27).

While Handa or Keller does not explicitly teach a method that employs the lipoxygenase gene encoding SEQ ID NO: 1, on page 3 of the latter reference, Handa teaches that some lipoxygenases are induced in response to pathogen/pest attach, suggesting a role in pathogen/pest resistance.

Veronesi et al teach the lipoxygenase gene encoding Applicant's SEQ ID NO: 1, and suggest transformation of tobacco plants with the gene to induce resistance against

Phytophthora parasitica (Ppn), a devastating crop pathogen.

It would have been obvious to one of ordinary skill in the art at the time the application was filed to use the method of transforming plants with a lipoxygenase gene for a desired trait as taught by Handa, and to modify that method by incorporating the elicitor induced tobacco lipoxygenase gene taught by Veronesi et al. One would have been motivated to preferably use the tobacco gene given its ability to induce resistance against fungal phytophthora, as taught by Veronesi et al. Therefore, the claimed invention as whole was *a prima facie* obvious.

Remarks

No claim is allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina A. Ibrahim whose telephone number is (571) 272-0797. The Examiner can normally be reached Monday -Thursday from 8:00AM to 5:30PM and every other Friday from 9:00AM to 5:00 PM. Before and after final responses should be directed to fax nos. (703) 872-9306 and (703) 872-9307, respectively.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Amy Nelson, can be reached at (571) 272-0804.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

5/16/05
Mai

MEDINA A. IBRAHIM
PATENT EXAMINER